

# Hyponatremia associated with sertraline and fluoxetine: A case report

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## Abstract

*The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a rare but serious adverse effect of the selective serotonin reuptake inhibitors (SSRIs). Although many case reports describe this association, few report the effect of rechallenge with another SSRI. We present a case of an elderly patient who developed hyponatremia with sertraline and SIADH when rechallenged with fluoxetine.*

## Introduction

As many as 15% of community-dwelling elderly Americans suffer from depressive symptoms and 1-3% suffer from major depression.<sup>1</sup> Tricyclic antidepressants are effective in the management of depression, however, their anticholinergic, alpha-1-adrenergic, and antihistamine effects limit their utility in many elderly patients. The selective serotonin reuptake inhibitors (SSRIs) have increasingly become the first-line therapy for depression because of their serotonin specificity. They are less likely to cause orthostatic hypotension, urinary hesitancy, and anticholinergic side effects, however, they commonly cause gastrointestinal upset and sexual dysfunction.

In the elderly, there has been an association between the SSRIs and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) a rare but potentially fatal adverse effect. Until recently, the incidence and risk factors for the development of SSRI-induced SIADH among the elderly was unknown. In a retrospective case control study of outpatients and inpatients in a rehabilitation service over the age of 65 who had been taking either fluoxetine or paroxetine, the incidence of hyponatremia was estimated to be 1 in 200 per year. A statistically significant lower body weight was observed between cases (mean 53.0 kg, 95% CI 46.5-59.5 kg) and controls (mean 64.5 kg, 95% CI 60.1-68.4 kg). There was no statistically significant difference in age between the groups and the mean time to develop hyponatremia was 18 days (range 4-64 days).<sup>2</sup> In another retrospective study of elderly patients admitted to an acute psychiatry ward who were given an SSRI (n=32), 25% developed hyponatremia, half of these were symptomatic, including one patient who died following status epilepticus.<sup>3</sup> These data, although limited by their small sample size, suggest that the incidence of hyponatremia in elderly patients on SSRIs is low among outpatients but may be higher among those requiring hospitalization for acute psychiatric management.

The diagnosis of SIADH induced by an SSRI should be made with the appropriate laboratory data and exclusion of other causes of SIADH (i.e. diseases of the pulmonary, nervous, renal, and endocrine organ systems, malignancy, and other medications). Although many case reports describe the relationship between SIADH and SSRIs, few report the effect of a rechallenge with an SSRI. We present a case of an elderly patient who developed hyponatremia while on sertraline and SIADH when rechallenged with fluoxetine.

## Case Report

A 94 year old man was diagnosed with major depressive disorder in August 1999 and was started on sertraline. His past medical history was significant for hypertension and unilateral supraclavicular fossa neurofibroma. His other medications included atenolol, nifedipine, and valsartan. Two months later, he complained of weakness and persistence of depressive symptoms. A serum sodium level at that time was 122 meq/L. His baseline sodium level had been between 132-140 meq/L over the past three years. Sertraline was discontinued because of hyponatremia. He returned in February 2000 with a complaint of poor appetite and fatigue. Serum sodium was 126 meq/L. He agreed to rechallenge with fluoxetine. One month later he complained of polydipsia, estimated to be 2-3 liters per day. He denied polyuria, polyphagia, weakness, lethargy, muscle cramps, or seizure. Physical examination was significant for weight of 46.8 kg and clinical euolemia. Serum sodium was 114 meq/L. He was admitted to the hospital for evaluation and management of hyponatremia.

SIADH was suspected and confirmed by laboratory testing (Table 1). Workup of SIADH included TSH, PSA, morning serum cortisol, cosyntropin stimulation test, fecal occult blood testing, chest x-ray, head CT, and renal ultrasound. All were within normal limits. Treatment began with fluid restriction (800 cc/day), infusion of 3% saline, and cessation of fluoxetine. Hypertonic saline was stopped when the sodium corrected to 122 meq/L the following day. Sodium chloride tablets 1 gm tid were then started and fluid restriction continued. On hospital day 6, sodium was 128 meq/L at which point fluoxetine was restarted. At discharge on hospital day 8, sodium corrected to 130 meq/L. He was discharged with instructions to limit fluid intake to 1000cc/day, sodium chloride tablets 1 mg tid, fluoxetine 10 mg qd, and nifedipine, valsartan, and atenolol as prior to admission. Serum sodium was 130 meq/L four days after discharge.

Table 1

Serum Sodium	114 meq/L
Serum Osmolality	250 mOsm/kg
Urine sodium	87meq/L
Urine osmolality	320mOsm/kg

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In July 2000, he presented for follow-up and complained of fatigue and irritable mood. He admitted to noncompliance with sodium chloride supplementation. In the interval since discharge, serum sodium had remained stable and his mood gradually improved. Serum sodium was 120 meq/L and he was admitted for management of hyponatremia. He was placed on fluid restriction, sodium chloride tablets as prior to admission, and fluoxetine was discontinued. Urine sodium was 97 meq/L and urine osmolality was 417 mosm/kg. At discharge on hospital day 4, serum sodium improved to 129 meq/L. He was restarted on fluoxetine 10 mg per day, water restriction, and sodium chloride tablets. At follow-up one week later he reported improved mood and serum sodium was 131 meq/L.

## Discussion

This elderly man developed hyponatremia with sertraline and when rechallenged with fluoxetine developed SIADH. With both sertraline and fluoxetine, depressive symptoms failed to improve at two months and one month, respectively. The temporal relationship between sertraline and hyponatremia and between fluoxetine and SIADH with a negative workup for an organic cause of SIADH suggested that this was due to the SSRIs. Of interest is that four months after stopping sertraline, hyponatremia had not completely corrected. The reason for this remains unclear. In addition, his weight was in the range that placed him at risk for the development of hyponatremia, and he developed it within the period noted in the study mentioned earlier.<sup>2</sup>

Therapy with fluoxetine and outpatient management of SIADH after his first hospitalization resulted in clinical improvement in depressive symptoms for this patient, the first time since taking an SSRI. A regimen of water restriction and sodium replacement maintained normal sodium levels until he became noncompliant with the sodium supplements. Depressive symptoms also returned with this episode of hyponatremia. Reinstating sodium supplementation led to improved mood again and allowed the patient to continue with fluoxetine therapy.

## Conclusion

SIADH is a rare and potentially fatal adverse effect of the SSRIs. It should be suspected when a patient fails to respond to an SSRI, have other symptoms of hyponatremia, or are noted to have asymptomatic hyponatremia. In this elderly man who developed hyponatremia with sertraline and SIADH with fluoxetine, he failed to show an improvement in depressive symptoms with either SSRI. A regimen of fluoxetine, water restriction, and sodium supplementation successfully improved his mood while maintaining a stable serum sodium level.

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